REMARKS

The present amendment is being submitted concurrently with a Request for Continued Examination.

Prior to the present amendment, Claims 1, 2, 4, 5, 20, 23 to 51, and 55 to 57 were pending. With the present amendment, Claims 58 to 63 were added. No claims have been cancelled or amended. The presently pending claims are Claims 1, 2, 4, 5, 20, 23 to 51, and 55 to 63.

Claims 59 to 63 were added to define applicants' invention in the form of unit dose claims. Support for these claims is found, for example, in Example 3 of the application.

Claim 58 was added to define the formulation as one in which the core is coated by a membrane coating which contains ammonio methacrylate co-polymer and which contributes to the particle a weight gain of about 8% of the weight of the core. Support for this amendment is found in the application, for example, in Examples 1 and 2 and in Claims 5 and 6 as filed originally.

Applicants note also that there existed clerical errors in Claim 28 as presented in applicants' Replies of March 11, 2004, November 18, 2004, and August 1, 2004 in that amendments made in a Reply, filed August 26, 2002, were not placed into the claim. This has been corrected above. As this correction is not an additional amendment, it is not depicted above as an amendment.

An early and favorable allowance is requested respectfully.

The Examiner is invited to telephone the undersigned to discuss matters that the Examiner believes may be relevant to placing the application in condition for allowance.

Respectfully submitted,

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August 1, 2005

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of T. Jeary, C. Morrissey, and P. Stark
Application No. 09/744,169 Group No. 1615
Filed April 19, 2001 Examiner S. Tran
Controlled-release Selective Serotonin Reuptake Inhibitor Formulations

(Atty. Docket No. P 24,622-A USA)

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on Monday, August 1, 2005.

Kathl P. Higgins
Kathleen P. Higgins

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REPLY UNDER 37 CFR §1.116 TO EXAMINER'S ACTION OF MARCH 31, 2005

Sir:

Applicants request entry of the following amendment.

In the Claims

1. (Currently Amended) A multiparticulate controlled release selective serotonin reuptake inhibitor (SSRI) formulation for oral administration, said formulation comprising particles, the cores of which comprise an SSRI which is fluvoxamine or a pharmaceutically-acceptable salt thereof, said core having thereon ~~which comprises particles of an SSRI selected from the group consisting of fluoxetine, fluvoxamine, paroxetine, and sertraline or a pharmaceutically acceptable salt thereof coated with~~ a rate-controlling membrane coating ~~polymer~~ which allows controlled release of said SSRI over a period of not less than about 12 hours following oral administration.

2. (Original) A formulation according to Claim 1, wherein the particles are pellets.

3. (Cancelled)

4. (Currently Amended) A formulation according to Claim 2 ~~3~~, wherein the rate-controlling membrane coating comprises a mixture of a major proportion of a pharmaceutically acceptable film-forming, water-insoluble polymer and a minor proportion of a pharmaceutically acceptable film-forming, water-soluble polymer in a selected ratio, the selected ratio of said water-insoluble polymer to said water-soluble polymer being effective to permit a SSRI release rate which allows controlled release of said SSRI over a period of not less than about 12 hours following oral administration.

5. (Currently Amended) A formulation according to Claim 4, wherein the rate-controlling membrane coating contains an ammonio methacrylate co-polymer.

20. (Previously Presented) A formulation according to Claim 1, wherein the core further comprises an organic acid, the SSRI component and the organic acid being present in a ratio of from 50:1 to 1:50.

21. (Cancelled)

22. (Cancelled)

23. (Currently Amended) A formulation according to Claim 1, wherein said membrane coating is present in an amount such that it contributes to the particle a weight gain of from about 4% to about 15% of the weight of the core and is formed from a lacquer substance comprising ammonio methacrylate copolymer and wherein the SSRI release rate from the particles exhibits the following *in vitro* dissolution pattern when measured using a USP type II dissolution apparatus (paddle) according to US Pharmacopeia XXII in 0.05 M phosphate buffer at pH 6.8:

(a) no more than about 15% of the total SSRI is released after 0.5 of an hour of measurement in said apparatus;

(b) no more than about 25% of the total SSRI is released after 1 hour of measurement in said apparatus;

(c) between about 20% and about 75% of the total SSRI is released after 2 hours of measurement in said apparatus;

(d) not less than about 75% of the total SSRI is released after 4 hours of measurement in said apparatus; and

(e) not less than about 85% of the total SSRI is released after 6 hours of measurement in said apparatus.

24. (Currently Amended) A formulation according to Claim 1, wherein said membrane coating is present in an amount such that it contributes to the particle a weight gain of from about 4% to about 15% of the weight of the core and is formed from a lacquer substance comprising ammonio methacrylate copolymer and wherein the SSRI release rate from the particles exhibits the following *in vitro* dissolution pattern when measured using a USP type II dissolution apparatus (paddle) according to US Pharmacopeia XXII in 0.05 M phosphate buffer at pH 6.8:

(a) no more than about 20% of the total SSRI is released after 4 hours of measurement in said apparatus;

(b) no more than about 45% of the total SSRI is released after 6 hours of measurement in said apparatus;

(c) between about 45% and 80% of the total SSRI is released after 8 hours of measurement in said apparatus;

(d) not less than about 70% of the total SSRI is released after 10 hours of measurement in said apparatus; and

(e) not less than about 80% of the total SSRI is released after 12 hours of measurement in said apparatus.

25. (Previously presented) A formulation according to Claim 1 in a form suitable for oral administration.

26. (Previously presented) A formulation according to Claim 1 in a form

suitable for oral administration and comprising a blend of said particles in admixture with an immediate release form of SSRI or a pharmaceutically acceptable salt thereof to ensure a rapid attainment of effective therapeutic blood levels.

27. (Previously presented) A formulation according to Claim 26, wherein the immediate release form of SSRI comprises pellets.

28. (Currently Amended) A formulation according to Claim 25, wherein said membrane coating is present in an amount such that it contributes to the particle a weight gain of from about 4% to about 15% of the weight of the core and is formed from a lacquer substance comprising ammonio methacrylate copolymer and wherein the SSRI release rate when measured *in vitro* using a USP type II dissolution apparatus (paddle) according to US Pharmacopoeia XXII in 0.05 M phosphate buffer at pH 6.8 substantially corresponds to the following dissolution pattern:

(a) no more than 20% of the total SSRI is released after 1 hour of measurement in said apparatus;

(b) no more than 60% of the total SSRI is released after 2 hours of measurement in said apparatus;

(c) not less than 20% of the total SSRI is released after 4 hours of measurement in said apparatus;

(d) not less than 35% of the total SSRI is released after 6 hours of measurement in said apparatus;

(e) not less than 50% of the total SSRI is released after 8 hours of measurement in said apparatus;

(f) not less than 70% of the total SSRI is released after 10 hours of measurement in said apparatus; and

(g) not less than 75% of the total SSRI is released after 12 hours of measurement in said apparatus.

29. (Currently Amended) A formulation according to Claim 25, wherein said membrane coating is present in an amount such that it contributes to the particle a weight gain of from about 4% to about 15% of the weight of the core and is formed from a lacquer substance comprising ammonio methacrylate copolymer and wherein the SSRI release rate from the particles exhibits the following *in vitro* dissolution pattern when measured using a USP type II dissolution apparatus (paddle) according to US Pharmacopeia XXII in 0.05 M phosphate buffer at pH 6.8:

(a) no more than about 20% of the total SSRI is released after 1 hour of measurement in said apparatus;

(b) no more than about 45% of the total SSRI is released after 2 hours of measurement in said apparatus;

(c) between about 20% and about 70% of the total SSRI is released after 4 hours of measurement in said apparatus;

(d) between about 35% and about 85% of the total SSRI is released after 6 hours of measurement in said apparatus;

(e) not less than about 50% of the total SSRI is released after 8 hours of measurement in said apparatus.

(f) not less than about 70% of the total SSRI is released after 10

hours of measurement in said apparatus; and

(g) not less than about 75% of the total SSRI is released after 12 hours of measurement in said apparatus.

30. (Currently Amended) A formulation according to Claim 1, wherein said membrane coating is present in an amount such that it contributes to the particle a weight gain of from about 4% to about 15% of the weight of the core and is formed from a lacquer substance comprising ammonio methacrylate copolymer and wherein the SSRI release rate from the particles exhibits the following *in vitro* dissolution pattern when measured using a USP type II dissolution apparatus (paddle) according to US Pharmacopeia XXII in 0.05 M phosphate buffer at pH 6.8:

(a) no more than about 50% of the total SSRI is released after 2 hours of measurement in said apparatus;

(b) not less than about 35% of the total SSRI is released after 6 hours of measurement in said apparatus; and

(c) not less than about 80% of the total SSRI is released after 22 hours of measurement in said apparatus.

31. (Previously Presented) A formulation according to Claim 4, wherein the core further comprises an organic acid, the SSRI component and the organic acid being present in a ratio of from 50:1 to 1:50.

32. (Previously Presented) A formulation according to Claim 5, wherein the core further comprises an organic acid, the SSRI component and the organic acid being present in a ratio of from 50:1 to 1:50.

33. (Previously presented) A method for the treatment of depression or obsessive compulsive disorder treatable with an SSRI, comprising administering to a patient suffering from one of said conditions a therapeutically effective amount of a multiparticulate controlled release SSRI formulation according to Claim 1.

34. (Previously presented) A method for the treatment of depression or obsessive compulsive disorder treatable with an SSRI, comprising administering to a patient suffering from one of said conditions a therapeutically effective amount of a multiparticulate controlled release SSRI formulation according to Claim 25.

35. (Currently Amended) A formulation according to Claim 2 ~~3~~, wherein the rate-controlling membrane coating comprises a pharmaceutically acceptable film-forming, water-insoluble polymer in an amount effective to obtain a controlled release of a SSRI over a period of not less than about 12 hours following oral administration.

36. (Previously presented) The formulation according to Claim 1, wherein said rate controlling polymer is SSRI-permeable.

37. (Previously presented) The formulation according to Claim 1, wherein said rate controlling polymer is SSRI-permeable and water soluable.

38. (Previously presented) The formulation according to Claim 1, wherein said rate controlling polymer is SSRI-permeable and water insoluable.

39. (Previously presented) The formulation according to Claim 25, wherein said formulation is in capsule form.

40. (Previously presented) The formulation according to Claim 25, wherein

said formulation is in tablet form.

Claims 41 to 44 (Cancelled)

45. (Previously presented) A method for the treatment of depression or obsessive compulsive disorder treatable with an SSRI, comprising administering to a patient suffering from one of said conditions a therapeutically effective amount of a multiparticulate controlled release SSRI formulation according to Claim 24.

46. (Previously presented) The formulation according to Claim 24, wherein said formulation is in tablet form.

47. (Currently Amended) A multiparticulate controlled release selective serotonin reuptake inhibitor (SSRI) formulation for oral administration, which comprises particles, the core of which comprises an SSRI which is fluvoxamine or a pharmaceutically-acceptable salt thereof, said core ~~of an SSRI selected from the group consisting of fluoxetine, fluvoxamine, paroxetine, and sertraline or a pharmaceutically acceptable salt thereof~~ coated with a rate-controlling polymeric acrylate or methacrylate lacquer substance which allows controlled release of said SSRI over a period of not less than about 12 hours following oral administration.

48. (Previously presented) A formulation according to Claim 47 wherein said substance is said acrylate lacquer.

49. (Previously presented) A formulation according to Claim 47 wherein said substance is said methacrylate lacquer.

50. (Previously presented) A formulation according to Claim 47 wherein

said substance is a lacquer which contains a mixture of said acrylate and methacrylate.

51. (Previously presented) A formulation according to Claim 47 wherein said substance is an acrylic resin comprising a copolymer of acrylic and methacrylic acid esters having a low content of quaternary ammonium groups.

Claims 52 to 54 (Cancelled)

55. (New) The formulation of Claim 1 wherein said membrane coating is present in an amount such that it contributes to the particle a weight gain of from about 4% to about 15% of the weight of the core and is formed from a lacquer substance comprising ammonio methacrylate copolymer and wherein.

56. (New) The formulation of Claim 55 wherein said weight gain is in an amount of 4%, 6%, 8%, 10%, 12%, or 15% of the weight of the core.

57. (New) A method for the treatment of depression or obsessive compulsive disorder treatable with an SSRI, comprising administering to a patient suffering from one of said conditions a therapeutically effective amount of a multiparticulate controlled release SSRI formulation according to Claim 55.

REMARKS

Reconsideration of the allowability of the present application in view of the above claim amendments and the following remarks is requested respectfully.

Discussion of the Claims

In his Action, the Examiner acted upon Claims 1 to 5, 20, 22 to 40, 45 to 51, 53, and 54 of the application, Claims 41 to 44 having been withdrawn previously from further consideration as being directed to non-elected species and Claims 6 to 19, 21, and 52 having been cancelled.

In the present Reply, Claims 3, 22, 41 to 44, 53, and 54 have been cancelled without prejudice. Claims 1, 4, 5, 23, 24, 28 to 30, 35, and 47 have been amended. Claims 55 to 57 have been added.

The claims pending presently are Claims 1, 2, 4, 5, 20, 23 to 40, 45 to 51, and 55 to 57.

Discussion of the Amendments

The current claims include two independent "formulation" claims, namely Claims 1 and 47. Claim 1 has been amended to provide antecedent basis for the phrase "the core", which is used in various dependent claims, and to clarify that the core has thereon a rate-controlling membrane coating. Claim 47 has been amended to be consistent with Claim 1 in the use of the phrase "the core". Support for these amendments is found in Claim 3, now cancelled.

Claims 1 and 47 have been amended also to define the active agent as being fluvoxamine or a pharmaceutically-acceptable salt thereof. Support for this is found in Claims 1 and 47 as they were prior to amendment.

Claims 23, 24, and 28 to 30 have been amended and Claims 55 to 57 have been added to define the formulation as one in which the rate-controlling membrane coating is present in an mount such that it contributes to the particle a weight gain of from about 4% to about 15% of the weight of the core and is formed from a lacquer substance comprising ammonio methacrylate copolymer. Claim 56 further defines the formulation as one in which the weight gain contributed is 4%, 6%, 8%, 10%, 12%, or 15% of the weight of the core. Support for the above amendments and for Claim 55 to 57 is found in the application at, for example, page 27, and in Claims 5 and 47.

Claims 4 and 35 have been amended to depend from Claim 2. Prior to amendment, these claims depended from now cancelled Claim 3. The recitations of Claim 3 are incorporated into Claim 2 by virtue of the amendment to Claim 1 from which Claim 2 depends.

Claims 3, 22, 41 to 44, 53, and 54 have been cancelled without prejudice.

An amendment of an editorial nature has been made to Claim 5.

Applicants submit that a new search does not need to be conducted and the amendments place the claims in better form for consideration on appeal. Applicants request, therefore, that the above amendments be entered.

Discussion of the Examiner's Section 102(e) Rejection

The Examiner rejected Claim 54 under Section 102(e) as being anticipated by U.S. Patent No. 5,958,458 Norling et al. This rejection has been rendered moot by the cancellation of this claim.

Discussion of the Examiner's Section 103 Rejection

The Examiner has rejected Claims 1 to 5, 20, 22 to 40, 45 to 51, 53, and 54 under Section 103(a) as being unpatentable over the disclosure of U.S. Patent No. 5,958,458 to Norling et al. in view of U.S. Patent No. 6,183,780 to van Balken et al.

The Examiner's rejection is traversed respectfully. To establish a *prima facie* case of obviousness, the Examiner must show that one skilled in the art would have expected that the invention would work for its intended purposes. MPEP § 2143. Applicants submit respectfully that the Examiner has failed to establish a *prima facie* case of obviousness.

There is nothing in the combined disclosures of the cited art to lead one skilled in the art to have a reasonable expectation the fluxoamine, when substituted for the anti-depressants used in the formulations disclosed by Norling et al., would be released in the release profile specified by the claims. The Examiner argues that there is such an expectancy since Norling et al. discloses formulations which are "identical" to those claimed. This, however, is not the case as Norling does not disclose the use of fluvoxamine. Instead, it discloses only the use of anti-depressants which are imipramine, nortriptyline or pririptylene [sic] (protriptylene) and discloses specifically only formulations comprising theophylline and the release profiles achieved by such formulations. Theophylline is not chemically similar to fluvoxamine, either in property or in structure. Different compounds are expected to have different release properties. Accordingly, one skilled in the art would not have assumed that, simply because Norling et al. discloses that theophylline is released from the formulations therein in a certain profile, fluvoxamine, when substituted for theophylline, would also be released in the same profile.

Further, Claims 23, 24, 28, 29, 30, and 55 to 58 recite specific release

profiles and recite that the membrane coating is present in defined amounts and comprises ammonio methacrylate copolymer. Nothing in the cited art would give rise to an expectancy that particles coated with a membrane present in the specified amounts and comprising ammonio methacrylate copolymer would allow for release of SSRIs (or their respective salts) in the profiles recited.

For the reasons recited above, applicants request respectfully that the Examiner withdraw his Section 103 rejection.

Discussion of the Examiner's Section 112 Rejection

The Examiner has rejected Claims 23, 24, and 28 to 30 under the enablement requirement of Section 112, first paragraph, because the Examiner does not consider the claims to be enabled with respect to formulations other than those in which the rate-controlling membrane coating comprises Eudragit® (ammonio methacrylate copolymer) and is present in an amount such that it contributes to the particle a weight gain of 4%, 6%, 8%, 10%, 12%, or 15% of the weight of the core. According to the Examiner, the application has shown only that those formulations exhibit the release profile specified by the claims.

Applicants have amended Claims 23, 24, and 28 to 30 to define the membrane coating as being present in an amount such that it contributes to the particle a weight gain of from about 4% to about 15% of the weight of the core and is formed from a lacquer substance comprising ammonio methacrylate copolymer. It is believed that this amendment will overcome the Examiner's rejection. Although the above range encompasses amounts other than the specified 4%, 6%, 8%, 10%, 12%, or 15% amounts, it is intuitive that, if a formulation which comprises a membrane coating which is present in those amounts exhibits the specified release profile, formulations which comprise a membrane coating which is present in amounts in between the above specified amounts must exhibit the specified release profile as well.

In any event, it is noted that Claim 56 has been added to define the formulations as comprising a membrane coating which is present in an amount such that it contributes to the particle a weight gain of 4%, 6%, 8%, 10%, 12%, or 15% of the weight of the core and as being formed from a lacquer substance comprising ammonio methacrylate copolymer.

Discussion of the Examiner's Election of Species Requirement

Applicants advise that new Claims 55 to 57 are readable on the elected species.

Conclusion

For the reasons expressed above, applicants request respectfully that the Examiner reconsider and withdraw his rejections. An early and favorable allowance is requested respectfully.

The Examiner is invited to telephone the undersigned to discuss matters that the Examiner believes may be relevant to placing the application in condition for allowance.

Respectfully submitted,

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